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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,247	02/27/2004	Shan Lu	07917-190001 / UMMC 03-30	9906

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EXAMINER	
SGAGIAS, MAGDALINE K	

ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,247	LU ET AL.	
	Examiner	Art Unit	
	MAGDALENE K. SGAGIAS	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,7,8,17,18,20-31 and 33* is/are pending in the application.

4a) Of the above claim(s) *20-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7,8,17,18 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/18/08 has been entered.

Applicant's arguments filed 7/18/087 have been fully considered. The amendment has been entered. Claims 1, 3, 7, 8, 17-18, 20-31, 33 are pending. Claims 20-31 are withdrawn. Claims 2, 4-6, 9-16, 19, 32, 34-37are canceled. Claims 1, 3, 7-8, 17-18, 33 are under consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 6, 17, 32, 34, rejection under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al, (US 6,448,389 B1; 2002) in view of Mach et al, (Journal of Virology, 11881-11892, 2000); Temperton (International Journal of Antimicrobial Agents, 19: 169-172, 2002) is withdrawn.

Claims 7-8, 11, 14, 18, 33, 36-37 rejection under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al, (US 6,448,389 B1; 2002) in view of Mach et al, (Journal of

Virology, 11881-11892, 2000); Temperton (International Journal of Antimicrobial Agents, 19: 169-172, 2002) as applied to claims 1, 3, 6, 17, 32, 34 above, and further in view of Theiler et al, (Journal of Virology, 2890-2898, 2002); Weis et al, (Vaccine, 18: (815-824, 2000) is withdrawn.

Claims 1, 34-35 rejection under 35 U.S.C. 103(a) as being unpatentable over Gonczol et al, (US 6,448,389 B1; 2002) in view of Mach et al, (Journal of Virology, 11881-11892, 2000); Weis et al, (Vaccine, 18: (815-824, 2000) and further in view of Endresz et al, (Vaccine 17: 50-58, 1999) is withdrawn.

Applicant's arguments are moot in view of the new grounds of rejections as set forth below.

Claims 1, 3, 7-8, 17-18, 33 are rejected under 35 U.S.C. 102(b) as anticipated by **Plotkin et al,** [EP 0389286 B1, Date of publication 26.09.1990 (IDS)] in view of **Endresz et al** [Vaccine, 19: 3972-3980, 2001 (IDS)]; **Mach et al,** [Journal of Virology, 11881-11892, 2000 (IDS)].

Claims 1, 3, 17 are directed to a composition comprising nucleic acid molecules, encoding different cytomegalovirus (CMV) polypeptides, wherein the nucleic acid molecules comprise nucleotide sequences encoding: CMV polypeptides that induce a neutralizing antibody response, wherein the CMV polypeptides comprise a glycoprotein complex II (gcII) or an antigenic fragment thereof; wherein the nucleic acid molecules comprise DNA plasmids. Embodiments limit the CMV polypeptides to human CMV (HCMV) polypeptides. Claims 7, 8, 18, 33 are directed a composition comprising a plurality of nucleic acid molecules, wherein the nucleic acid molecules comprise nucleotide sequences encoding different human cytomegalovirus (HCMV) polypeptides that induce a neutralizing antibody response, wherein the HCMV polypeptides comprise: glycoprotein M (gM), or an antigenic fragment of gM, and

glycoprotein N (gN), and or an antigenic fragment of gN; wherein the nucleic acid molecules comprise DNA plasmids.

Plotkin et al teach a composition comprising an adenovirus encoding different human cytomegalovirus (HCMV) subunits for use of the glycoprotein gB subunit ofthis vaccine, and other subunits of HCMV which may be employed in the production of a vaccine selected from the gA/gB, or **gcII** as in the instant invention or gcIII or immediate early subunits of the human virus (column 4, lines 18-25) **(claim 3).** Plotkin et al teach a human cytomegalovirus subunit protein produced by an adenovirus expression vector, comprising a human cytomegalovirus (HCMV) vaccine, in that the subunit protein is gcII, and the subunit protein is produced in an adenovirus vector under the control of an expression control sequence, said virus being capable of expressing said subunit in vitro in a host cell or in vivo in a human (column 8 under claims). Plotkin et al teach the recombinant adenovirus containing the gcII, it is in orally administrable unit dose form for use as a vaccine in a pharmaceutical carrier (column 8 under claims) **(claims 17-18)**. Plotkin et al teach the recombinant virus may also contain multiple copies of the HCMV subunit, or alternatively, the recombinant virus may contain more than one HCMV subunit type, so that the virus may express two or more HCMV subunits or immediate-early antigens and subunits together (column 4, lines 50-55) **(claim 33).** Plotkin teaches the inoculation of Ad5/gB (gB a HCMV subunit) immunization in hamsters induced neutralizing antibody to HCMV as detected by the plaque-reduction neutralization assay (column 7, lines 36-50). Plotkin suggests the vaccine is expected to provide analogous results in humans as in the hamster model, i.e. production of neutralizing antibody and also like the HCMV gB subunit of gcII subunit of the HCMV may be expressed in a recombinant adenovirus with analogous results (column 7 lines 50-55, column 8, lines 1-8). Plotkin differs from the present invention for not teaching a plasmid for the gcII (gN and gM) vaccine composition.

However, at the time of the instant invention Endresz et al, teach optimization of DNA immunization against human CMV (title). Endresz et al, discusses several approaches have been used to develop an effective and safe subunit HCMV vaccine and recombinant adeno-, vaccinia-, and canarypox-viruses expressing the gB or IE proteins induced antibody and CTL responses specific to the inserted genes in experimental animals, whereas, the canarypox-gB recombinant induced no or only minimal levels of gB-specific antibodies in humans, it did prime the antibody response for a Towne strain-booster (p 3972, 2nd column bridge p 3973, 1st column). Endresz et al, teach that mice injected with plasmids carrying the full length membrane anchored glycoprotein gB of the HCMV or the secreted forms of the glycoprotein gB of the HCMV the secreted form induced higher significantly higher antibody titers than the plasmid carrying the membrane bound form of gB and moreover priming with the plasmid carrying the secreted gB form followed by boosting with the gB protein subunit resulted in high neutralizing antibody response than the membranous gB form (abstract; figure 3; and under results). Endresz et al, suggest for high neutralizing antibody responses by priming with plasmid secretory form gB of HCMV followed by gB protein boost in mice might be suitable in human immunization as compared to parallel viral protocols (p 3977, 2nd column). **Mach et al,** supplement the teachings of Endresz by teaching thus far the gB and gH have been identified as major targets for the neutralizing immune response in human but additional antigens must contribute to the induction of neutralizing antibodies based on preabsorbption studies of human sera with gB or gH (p 11891, 1st column). Mach et al teach glycoprotein gM (UL100) and gN (UL73) of the gcll form a complex in Cos cells cotransfected with the plasmid gM (UL100) and the plasmid gN (UL73) allowing the transport of the gM-gN complex to the compartments of the secretory pathway (figure 3). Mach et al teach the gM-gN complex reactivity with sera from HCMV-seropositive donors, whereas most sera failed to react with either gM or gN when

expressed alone, 62% of sera were positive for the gM-gN complex and because a murine monoclonal antibody reactive with gN in the gM-gN complex efficiently neutralizes infectious virus, the gM-gN complex may represent a major antigenic target of antiviral antibody responses (abstract). As such Mach taken with Endresz provide sufficient motivation for one of ordinary of skill in the art to replace the adenovirus carrying the gB subunit of gcII with the plasmid gM(UL100) and gN(UL73) of Mach for priming with said plasmids and boost with their recombinant protein as taught by Endresz.

Accordingly, in view of the teachings of Plotkin, it would have been obvious for one of ordinary skill in the art, at the time the claimed invention was made, to replace the HCMV gB subunit of gcII adenovirus of Plotkin with plasmid gM (UL100) and gN (UL73) of Mach for priming with said plasmids and boost with their recombinant proteins as taught by Endresz for a vaccine in humans for inducing neutralizing antibodies against HCMV with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification as Plotkin suggests production of neutralizing antibody like the HCMV gB subunit of gcII vaccine is expected to provide analogous results in humans as in the hamster model, and since the plasmid carrying the secreted gB form followed by boosting with the gB protein subunit resulted in high neutralizing antibody response than the membranous gB as taught by Endresz. One of ordinary of skill in the art would have been particularly motivated to use plasmid gM (UL100) and the plasmid gN (UL73) for priming as taught Endresz and since the gM-gN complex is the secreted form as taught by Mach and moreover since the secreted form is better for priming than the membranous form for the production of neutralizing antibodies against HCMV as taught by Endresz. Moreover, one of ordinary of skill in the art would have been particularly motivated to replace the adenovirus of Plotkin with the plasmid technology of the Endresz/Mach since Endresz teaches priming with plasmid containing the secreted form of

the HCMV subunit increases the humoral immune response neutralizing antibody of the IgG2a which is associated with Th1 response (cellular immune response) and Mach suggests that the gM-gN complex may represent a major antigenic target for antiviral antibody responses and a highly immunogenic structure for the humoral immune response during natural infection (p 11882, 1st column, 2nd paragraph).

Thus, the claimed invention as a whole, is clearly prima facie obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Magdalene K. Sgagias whose telephone number is (571) 272-3305. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, Jr., can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

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